PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4-32586A	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/IB 03/01985	International filing date *(day/month/year)* 23.05.2003	Priority date *(day/month/year)* 24.07.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/506		
Applicant NOVARTIS AG		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
24.01.2004	09.07.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Ludwig, G Telephone No. +49 89 2399-8698

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IB 03/01985

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-16 as originally filed

Claims, Numbers

1-8 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-8
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-8
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-8 (cf. text)
	No:	Claims	

2. Citations and explanations

see separate sheet

D1: J.Clin.Endocrinology & Metabolism 88, 1889-1896 (2003) - **P-document**
D2: Database Biosis Abstract no. PREV200300111240
Surgery 132, 960-967 (2002) - **P-document**

D3: Ann. Med. 33, 451-455 (2001)
D4: WO 99/03854

Item V:

1. If the priority of the application is not valid (not checked) document D1 and D2 (articles) can be used against novelty/Inventive step of the claimed subject-matter.

2. The use of compound I free base and compound I mesylate ("Imatinib mesylate"=Gleevec=Glivec=STI571=STI-571) for the treatment of cancer is known from documents D3-D4.

Document D3 is a review article about Imatinib as an anticancer agent for solid tumours which discloses the known activity of this compound against chronic myeloid leukemia, Philadelphia chromosome-positive acute lymphoblastic leukemia and gastrointestinal stromal tumours.
Imatinib is a known inhibitor of a few tyrosine kinases including KIT.
D3 states that "KIT may be overexpressed in many types of human solid tumours, such as small-cell lung carcoinoma, melanoma, seminoma, some carcinomas, and adenoid cystic carcinomas, *but the role of KIT in the pathogenesis of these tumours is not yet known.*" (emphasis added by the International Preliminary Examining Authority).

D4 indicates that imatinib is active against gliomas, sarcomas, prostate tumours, and tumours of the colon, breast, and ovary and against BCR-abl-positive cancer and tumour diseases such as leukemias but no pharmacological experimental data are contained in this document.

The problem to be solved by the invention was the provision of a medicament which is effective against anaplastic thyroid carcinomas.

In view of the relevant state of the art documents D3 and D4 as described above it

appears that there was no way to know at the priority date with a reasonable degree of certainty if imatinib could also be effective against anaplastic thyroid carcinoma, i.e. there was no reasonable expectation of success.

The applicant has shown the effectiveness of imatinib against thyroid anaplastic carcinomas both by in vitro and in vivo experiments.

In view of the above an inventive step can be acknowledged for subject-matter claimed in claims 1-8.

3. For the assessment of the present claims 3-8 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.